Receipt

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231 on May 22, 2002.

David Saliwanchik

David R. Saliwanchik, Patent Attorney

Patent Application
Docket No. SPO-112
Serial No. 09/762,842

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Akira Murasugi, Yukio Asami, Isao Kido, Hideshi Kumai
Serial No.	:	09/762,842
Conf. No.	:	1096
Filed	:	February 12, 2001
For	:	High Level Secretory Expression System of Intact MK Family Protein

Office of Initial Patent Examination
Customer Service Center
Commissioner of Patents and Trademarks
Washington, D.C. 20231

REQUEST FOR CORRECTION OF FILING RECEIPT

Sir:

The applicants respectfully request the correction of error in the official Filing Receipt for the above-identified patent application. A clerical error has occurred in the title of the application. The correction needed is as follows:

Title

High Level Secretory Expression of Intact MK Family Protein

should read

High Level Secretory Expression System of Intact MK Family Protein

A copy of the erroneous Official Filing Receipt accompanies this Request. Also, attached is a copy of page 1 of the Transmittal Letter Form PTO-1390 and page 1 of the subject specification. Correction of the above is respectfully requested.

Respectfully submitted,

David Saliwanchik

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DRP/la
Enclosures: Copy of erroneous Filing Receipt;
Page 1 of Form PTO-1390; and
Page 1 of subject application.

DESCRIPTION

HIGH LEVEL SECRETORY EXPRESSION SYSTEM OF INTACT MK FAMILY PROTEIN

Technical Field

The present invention relates to a high level secretory expression system of an intact MK family protein by recombinant DNA techniques using methylotrophic yeast as the host.

Background Art

MK is a growth factor discovered as the retinoic acid responsive gene product, and is a polypeptide that is rich in basic amino acids and cysteine and that has the molecular weight 13 kDa (Kadomatsu, K. et al.: Biochem. Biophys. Res. Commun., 151: 1312-1318, 1988; Tomomura, M. et al.: J. Biol. Chem., 265: 10765-10770, 1990). MK has 45% sequence homology to another heparin-binding protein referred to as pleiotrophin (PTN) or heparin-binding growth associated molecule (HB-GAM).

MK and PTN have common activities such as the neurotrophic factor activity (Li, Y.-S. et al.: Science, 250: 1690-1694, 1990; Merenmies, J. & Rauvala, H.: J. Biol. Chem., 265: 16721-16924, 1990; Muramatus, H. et al.: Dev. Biol., 110: 284-296, 1985), the enhancement of fibrinolytic system (Kojima, S. et al.: J. Biol. Chem., 270: 9590-9596, 1995), proliferation of various cells, transformation of NIH3T3 cells (Kadomatus, K. et al..: Brit. J. Cancer, 75: 354-359, 1997; Yokota, C. et al.: J. Biochem., 123: 339-346, 1998), and angiogenesis.

Thus, these MK family proteins are expected to be useful as drugs, and the development of high level expression system of these proteins has been strongly demanded. Natural MK and PTN proteins are not glycosylated. Therefore, the high level expression of these proteins with no glycosylation by recombinant DNA techniques, would be extremely useful not only for production of the proteins as drugs but also for structural and functional analyses of the proteins. In this invention, an unglycosylated MK family protein is referred to as an intact MK family protein. Herein, an MK family protein means a protein comprising at least the amino acid sequence of a mature

FORM PTO-1390 REV. 10/2000 U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTORNEY'S DOCKET NUMBER
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371	320-112 U.S. APPLICATION NO. (If known, see 37 CFR)

INTERNATIONAL APPLICATION NO	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/JP99/04332	10 August 1999	26 March 1999 10 August 1998

TITLE OF INVENTION: High Level Secretory Expression System Of Intact MK Family Protein

APPLICANT(S) FOR DO/EO/US: Akira Murasugi, Yukio Asami, Isao Kido, Hidesh Kumai

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [X] This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. [ ] This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. [X] This is an express request to promptly begin national examination procedures (35 U.S.C. 371(f)).
4. [X] The US has been elected by the expiration of 19 months from the priority date (PCT Article 31).
5. [X] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [ ] is attached hereto (required only if not communicated by the International Bureau).
   b. [X] has been communicated by the International Bureau.
   c. [ ] is not required, as the application was filed in the United States Receiving Office (RO/US).
6. [ ] An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
7. [ ] Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. [ ] are attached hereto (required only if not communicated by the International Bureau).
   b. [ ] have been communicated by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [ ] have not been made and will not be made.
8. [ ] An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C.371(c)(3)).
9. [X] An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). (unsigned)
10. [ ] An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11 to 16 below concern document(s) or information included:

11. [ ] An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. [ ] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. [X] A FIRST preliminary amendment.
    [ ] A SECOND or SUBSEQUENT preliminary amendment.
14. [ ] A substitute specification.
15. [ ] A change of power of attorney and/or address letter.
16. [X] Other items or information. Submission of Sequence Listing Under 37 CFR 1.821-1.825